



## A PILOT STUDY ON EFFICACY OF TADALAFIL IN BPH PATIENTS

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### ABSTRACT

**Background:** Benign prostatic hyperplasia (BPH) is the most common benign tumour in men and is responsible for urinary symptoms in the majority of males over the age of 50 years. **Aim:** Aim of this study is to assess the efficacy of Tadalafil 5mg OD in BPH patients. **Objective:** To assess the efficacy of Tadalafil in Benign Prostatic Hyperplasia patients. To describe the social and demographic clinical features of BPH patients. **Materials and Method:** The efficacy of Tadalafil will be assessed in 15 patients using International prostate symptom score questionnaire and the patients will be asked to review after one months of drug therapy. **Results and Discussion:** Tadalafil 5mg OD has significant effect on IPSS score( $t = 11.64$ ). **Conclusion:** Tadalafil 5mg OD is clinically significant in the improvement in LUTS secondary to BPH and there was an significant improvement in the IPSS score.

**KEYWORDS:** Benign prostatic hyperplasia (BPH), Lower urinary tract symptoms(LUTS), Tadalafil.

### INTRODUCTION

Benign prostatic hyperplasia (BPH) is the most common benign tumour in men and is responsible for urinary symptoms in the majority of males over the age of 50 years. Autopsy studies have revealed the histological presence of BPH in 50% of males aged 51–60 years, increasing to 90% in those over 85. By the age of 80 years, virtually all men exhibit one or more of the symptoms associated with BPH.<sup>[3]</sup> The etiology of BPH include obstruction of the bladder neck caused by an enlarged prostate gland, excessive stimulation of  $\alpha$ -adrenergic receptors in the smooth muscle of the prostate, urethra, and bladder neck or irritability of hypertrophied detrusor muscle as a result of long-standing bladder outlet obstruction.<sup>[1]</sup>

Drug treatment goals for benign prostatic hyperplasia include relieving obstructive and irritative voiding symptoms, preventing complications of disease, and reducing the need for surgical intervention. Single-drug treatment with an  $\alpha$ -adrenergic antagonist like Doxazosin, Prazosin is preferred for patients with moderate symptoms of benign prostatic hyperplasia. Single-drug treatment with a 5 $\alpha$ -reductase inhibitor like Dutasteride, Finasteride should be reserved for patients with significantly enlarged prostates of at least 40g.<sup>[1,14]</sup> These drugs are clinically effective in treating BPH but have certain side effects like sexual dysfunction, dizziness, hypotension, headache.

Several studies reported that ED and BPH are associated epidemiologically and can have common patho-

physiological pathway, since then PDE-5 inhibitors like Sildenafil, Tadalafil, Vardenafil have received increased attention for treating BPH.<sup>[2,8]</sup> Tadalafil is initially given for ED and found to be effective in BPH with ED.<sup>[6]</sup> The mechanism of action of long acting PDE -5 inhibitor Tadalafil in the treatment of men with LUTS secondary to BPH is believed to be associated with stimulation of increased activity of NO or CGMP pathway via inhibition of PDE- 5 isoenzymes in different tissues of the lower urinary tract. This results in smooth muscle relaxation in the bladder, urethra, prostate and supporting vasculature, Increased blood perfusion to the pelvic area and Modulation of sensory stimuli from this area.<sup>[4,7]</sup> The objective of present study is to assess the efficacy of Tadalafil (5mg- OD) in patients with BPH.

### MATERIALS AND METHODS

The present study was conducted after clearance from the Institutional Human Ethical committee.

It was carried out in the Urology department of a tertiary care center.

### INCLUSION CRITERIA

- Patients who are willing to participate in the study.
- International Prostate Symptom Score of  $\geq 8$ .
- Peak urine Flow Rate  $< 15$  ml/sec.
- Patients of age group greater than 50 yrs.

**EXCLUSION CRITERIA**

- Patients with raised Serum Prostate Specific Antigen level(>20ng/ml)/ suspected prostatic malignancy.
- Post Void Residual Urine of >200ml.
- Patients who received recent 5 alpha reductase inhibitors.
- History of lower urinary tract malignancy /pelvic surgery.
- Neurological conditions causing bladder dysfunction, hepato-renal insufficiency.

**PROCEDURE**

Only fifteen patients diagnosed with BPH were enrolled for the study. A written informed consent was taken from the patients as per ICMR biomedical research guideline format. All relevant information regarding the study were collected from case records and direct interview with patients with the help of physician. Data was collected by using a suitably designed proforma. The efficacy of Tadalafil was assessed using Ultrasound scan and International Prostate Symptom Score questionnaire and the patients were asked to review after one month of drug therapy. Based on International Prostate Symptom Score, Patients were categorized into mildly symptomatic (score 0-7), moderately symptomatic (score 8-19) and severely symptomatic (score 20-35). International Prostate Symptom Score was evaluated after the drug therapy IPSS score includes incomplete emptying, frequency, intermittency, urgency, weak stream, straining, nocturia and USG was also evaluated which includes prostate volume and residual volume. At the end of the study all the parameters and scores were compared from base line to end of the study.

**RESULTS AND DISCUSSION**

Fifteen patients having LUTS due to BPH diagnosed by physicians where enrolled in the study. The study was done in the urology department of a tertiary care hospital in south kerala. Patients between the age of 50-80 where enrolled in the study. Out of 15 patients 7 patients had BPH with Erectile dysfunction and 8 patients had BPH without Erectile dysfunction.

The data regarding personal information and different parameters of IPSS questionnaire and USG before and after intervention were collected and calculated basic descriptive statistics such as mean, standard deviation, frequency and percentages.

The effectiveness of treatment was statistically assessed using paired T test. A calculated p-value less than 0.05 is considered to be statistically significant. The details given are as follows

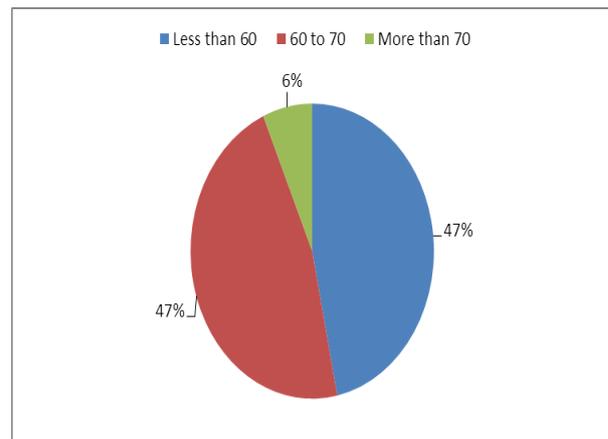
Distribution of patients based on age is shown in table 1.

**Table 1: based on the distribution of patients based on age.**

AGE	FREQUENCY	PERCENTAGE
<60	7	46.7
60-70	7	46.7
>70	1	6.6

From table it is seen that 46.7% patients are <60 and 60-70years of age group and 6.6% in more than 70 years of age. Majority of patients selected in the sample are 50-70 years of age group.

The diagrammatic representation of age distribution of patients are shown in figure 1.

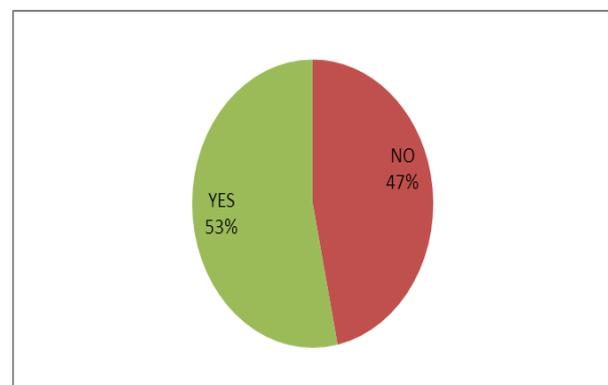


**Figure 1: diagrammatic representation of age distribution of patients.**

**Table-2 Distribution of patients based on Erectile Dysfunction.**

Erectile Dysfunction	Frequency	Percent
NO	7	46.7
YES	8	53.3
Total	15	100

From table 2 it is seen that out of 15 patients 46.7% of the pts don't had Erectiledysfunction and 53.3% had Erectile dysfunction. ie majority of patients had the problem of erectiledysfunction.



**Figure 2: The diagrammatic representation of table 2 is shown in figure.**

Distribution of patients based on the duration of LUTS is shown in table -3.

Disease duration (days)	Frequency	Percentage
60.00	5	33.3
90.00	3	20.0
120.00	3	20.0
150.00	1	6.7
180.00	1	6.7
240.00	1	6.7
280.00	1	6.7
<b>Total</b>	15	100.0

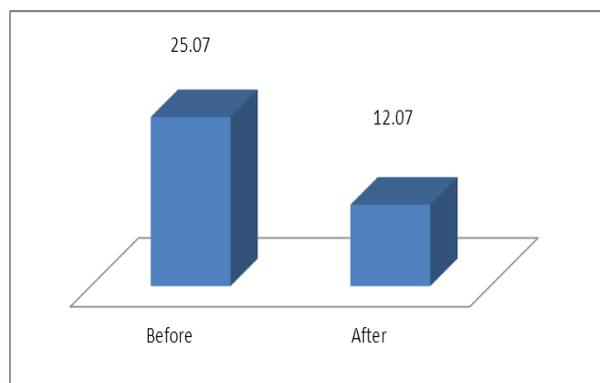
From the table 3 it is seen that 33.3% patients had a duration of 60days and 20% had a duration of 90-120 days and other had a duration of 6.7% Change in total IPSS score from baseline to 4 weeks after treatment. LUTS treated with Tadalafil 5 mg once daily has resulted in statistically significant improvements as assessed by total IPSS is shown in table 4.

**Table 4: Effectiveness of treatment on total IPSS score**

Variable	Test	Mean	Standard Deviation	Percentage Change	T	P value
IPSS	BEFORE	25.07	5.23	51%	11.64	0.00
	AFTER	12.07	3.77			

From table-4 paired t-test showed that treatment has significant effect on total IPSS score ( $t=11.64$ ), ( $p,0.01$ ) that is before the treatment mean of total IPSS score was 25.07 with standard deviation 5.22 and after the treatment it significantly reduced to a mean 12.07 with standard deviation 3.77 having more than 50% increase in efficacy.

The diagrammatic representation of change in IPSS score before and after treatment is shown in figure 3.



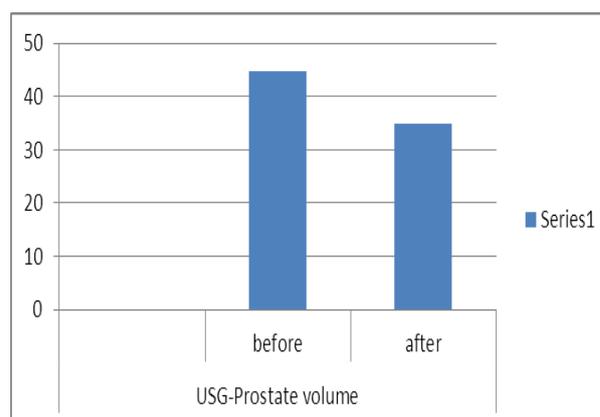
**Figure 3: Diagrammatic representation of change in IPSS score before and after treatment.**

**Table 5: Effectiveness of treatment on ultrasound scan.**

Variable	Test	Mean	Standard Deviation	Percentage change	t value	P value
USG (prostate volume)	Before	44.86	8.08	22.82	7.54	0.00
	After	34.80	5.54			

From table 5 paired t-test showed that treatment has significant effect on USG ( $t = 7.54$ ), ie before treatment mean of prostate volume was 44.86 with standard deviation 8.08 and after the treatment it significantly reduced to mean of 34.80 with SD 5.54 which shows increase in efficacy.

The diagrammatic representation of mean of USG – prostate volume before and after treatment is shown in figure 4.



As shown in our paired T test, tadalafil 5mg OD is found to be statistically significant for relieving LUTS/BPH as measured by IPSS. Gacci M, Anderson K E et al. has been postulated an association between BPH and Erectile dysfunction.<sup>[13]</sup> Dr. Puneet Mahajan et al. postulated that tadalafil 5mg OD has clinically meaningful and statistically significant in LUTS secondary to BPH.<sup>[2]</sup>

Dmochowski R, et al explored the impact of Tadalafil on uro-dynamic parameters in patients of LUTS secondary to BPH in randomized, placebo control clinical trial. Treatment with Tadalafil resulted in significant improvement in IPSS (mean difference between treatments – 4.2,  $p < 0.001$ ), in their study. No negative impact on bladder function as measured by detrusor pressure at Vmax or any other assessed uro dynamic parameter was seen in this study.<sup>[15]</sup> Yang Dong et al. postulated that tadalafil showed good efficacy and safety for improving LUTS and erectile dysfunction in men with BPH and 5mg of tadalafil significantly improved quality of life.<sup>[5]</sup> Roehrborn and colleagues [Roehrborn *et al.* 2008] reported data from a dose finding study with tadalafil in men with ED and LUTS.<sup>[10]</sup> Egerdie and colleagues [Egerdie *et al.* 2012] assessed the effects of tadalafil 2.5 or 5 mg once daily on ED and BPH-associated LUTS in 606 men with both conditions in a multinational, double-blind, placebo-controlled study.<sup>[11]</sup> Recently, three papers provided analysis of pooled data from four randomized, double-blind, placebo-controlled, 12-week, parallel-design, multinational LUTS/BPH studies assessing the efficacy and safety of tadalafil once-daily for LUTS/BPH [Roehrborn *et al.* 2008; Porst *et al.* 2011] or LUTS/BPH and ED [Egerdie *et al.* 2012].<sup>[10,11,12]</sup> This is important to know since LUTS are a chronic condition and treatments must be efficacious also in the long-term. In this context, Donatucci and colleagues [Donatucci *et al.* 2011] reported on the long-term efficacy of tadalafil.<sup>[9]</sup>

## CONCLUSION

Tadalafil 5mg OD is clinically significant in the improvement in LUTS secondary to BPH and there was a significant improvement in the IPSS score. Tadalafil 5mg OD is approved by FDA for the treatment of LUTS in men and also approved for the treatment of ED. Tadalafil 5mg OD is the only drug available to treat LUTS and ED conditions simultaneously. The sexual dysfunction caused by  $\alpha$ -adrenergic agonist and  $5\alpha$ -reductase inhibitors are avoided by tadalafil.

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